JAMA Neurol. 2015 Jan;72(1):88-95. doi: 10.1001/jamaneurol.2014.2472.

Combined rasagiline and antidepressant use in Parkinson disease in the ADAGIO study: effects on nonmotor symptoms and tolerability.

Smith KM[1], Eyal E[2], Weintraub D[3]; **ADAGIO** Investigators.

Collaborators (130)

Author information

Abstract

IMPORTANCE: Depression, cognitive impairment, and other **nonmotor symptoms** (NMSs) are common early in **Parkinson disease** (PD) and may be in part due to **disease**-related dopamine deficiency. Many patients with PD are treated with antidepressants for NMSs, and the effect of the combination of PD medications that enhance dopamine neurotransmission and antidepressants on NMSs has not been studied. We report the **effects** of the addition of a monoamine oxidase B inhibitor, **rasagiline**, to **antidepressant** treatment in PD.

OBJECTIVE: To evaluate the effect of **rasagiline** on depression, cognition, and other PD NMSs in patients taking an **antidepressant** in the Attenuation of **Disease** Progression With Azilect Given Once Daily (**ADAGIO**) **study**.

DESIGN, SETTING, AND PARTICIPANTS: The **ADAGIO study** was a double-blind, placebo-controlled, delayed-start trial of **rasagiline** in de novo PD. In this exploratory post hoc analysis, we analyzed patients taking an **antidepressant** during the 36-week phase 1 period, in which patients were randomized to **rasagiline** (1 or 2 mg/d) or placebo.

MAIN OUTCOMES AND MEASURES: We evaluated the change in NMSs in patients taking an **antidepressant** and **rasagiline** compared with those taking placebo. The NMSs were assessed by Movement Disorder Society-sponsored revision of the Unified **Parkinson**'s **Disease** Rating Scale **Nonmotor** Experiences of Daily Living, the original Unified **Parkinson**'s **Disease** Rating Scale, and the **Parkinson** Fatigue Scale.

RESULTS: A total of 191 of the 1174 patients (16.3%) were treated with antidepressants during phase 1 and provided efficacy data. Depression and cognition scores revealed significantly less worsening in the **rasagiline** group compared with the placebo group (differences in Movement Disorder Society-sponsored revision of the Unified **Parkinson**'s

Disease Rating Scale item-adjusted means [SEs], -0.19 [0.10], P = .048, and -0.20 [0.05], P < .001, respectively). **Parkinson** Fatigue Scale (mean [SE] difference, -0.42 [0.09], P < .001) and daytime sleepiness (mean [SE] difference, -0.24 [0.09], P = .006) scores also revealed significantly less worsening in the **rasagiline** group compared with placebo. There was a nonsignificant trend toward less worsening in apathy and no significant between-group differences in anxiety or sleep. The effect on depression remained significant after controlling for improvement in motor **symptoms** (mean [SE] difference, -0.23 [0.09], P = .009). There were no serious adverse events in the **combined rasagiline-antidepressant** group suggestive of serotonin syndrome.

CONCLUSIONS AND RELEVANCE: The combination of **rasagiline** and antidepressants in patients with de novo PD is associated with reduced worsening of a range of NMSs in preliminary analyses. Adverse **effects** appear uncommon with this combination. These findings suggest a role for dopamine-enhancing therapies in NMSs in early PD and encourage further **study** and confirmation.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00256204.

PMID: 25420207 DOI: 10.1001/jamaneurol.2014.2472

[Indexed for MEDLINE]

Publication types, MeSH terms, Substances, Secondary source ID

LinkOut - more resources